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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/875,361	Applicant(s) Chang
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 4, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-10 and 14-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-10 and 14-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. A new and non-final office action follows.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 2, 5-9, 14-19, and 21-24 are rejected under 35 U.S.C. 103(a) over Mao et al. (Chinese Patent CN 1314493) (March 20, 2000) in view of Vermeulin et al. (U.S. Patent

6,172,261 B1) (January 9, 2001) further in view of Cruickshank (U.S. Patent 6,194,563 B1) (February 27, 2001).

Mao et al teach a herbal chip comprising a plastic slide, a coating on the plastic slide which binds fractions or components obtained from herbs (Arabidopsis thaliana in this case) to the slide in independently allocated microarrays on the coating, wherein the coating comprises an amino group (Claims 1-4 and Page 12, line 4 to page 14, line 2 and Figures 1-3).

Mao et al inherently teach a method of using the chip for screening for active ingredients in herbs, comprising the steps of loading a labeled probe(s)-containing solution onto the chip for conducting hybridization, and imaging and identifying the gridded samples that react with or bind to the labeled probe (Page 12, line 4 to page 14, line 2 and Figures 1-3 and Claims 5-6).

Mao et al teach a chip comprising a plastic slide, a coating as a spacer on the plastic slide and fractions or components independently allocated in microarrays on the coating (Figures 1-3).

Mao et al teach a chip, wherein the plastic slide is made of two cavity chambers (Figures 1-3).

Mao et al teach a method of producing the chip, comprising the steps of preparing a plastic slide, coating the surface of the plastic slide with amino groups, and spotting and immobilizing on the coated plastic slide a massive amount of samples in a gridded area in microarrays, wherein each sample contains fractions or ingredients obtained from the herb (Claims 1-6 and Page 10, line 7 to page 14, line 2 and Figures 1-3).

Mao et al teach a method, wherein the samples are spotted or immobilized on the surface of cavity chambers (Figures 1-3).

Mao et al teach a method, wherein the label is a dye (Page 13, first paragraph).

Mao et al teach a method, wherein the labeled probe(s)-containing solution is heterogeneous (Page 8, lines 10-11).

Mao et al do not teach a chip, wherein the material of the plastic slide is a copolymer made of ethylene, propylene or styrene.

Vermeulin et al. teach a chip, wherein the material of the plastic slide is a copolymer made of ethylene, propylene or styrene (Column 31, lines 6-14).

Mao et al do not teach a chip, wherein the coating is made of polyfunctional molecules.

Vermeulin et al. teach a chip, wherein the coating is made of polyfunctional molecules (Abstract and Column 33, lines 30-67 and Figures 29-31) (polyamine in this case).

Mao et al do not teach a method, wherein the plastic slide is pretreated with a polyfunctional aldehyde glutaraldehyde followed by soaking in a solution of NH2 groups-providing precursor before coating the plastic slide.

Vermeulin et al. teach a method, wherein the plastic slide is pretreated with a polyfunctional aldehyde glutaraldehyde followed by soaking in a solution of NH2 groups-providing precursor before coating the plastic slide (Column 33, lines 49-52).

Vermeulin et al. teach a method, wherein the labeled probe(s)-containing solution is heterogeneous.(Column 33, lines 60-67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the chip containing polyamine analogues as therapeutic and diagnostic agents of Vermeulin et al. in the herbal chip of Mao et al. since Vermeulin et al. state, "The assays of the invention are useful for high throughput screening of targets in the discovery of drugs that interact with the polyamine system (Abstract, last sentence)." Moreover , Mao et al state, "The diagnosis chip technique is a molecular diagnosis method combining DNA hybridization technique and fluorescent marking technique, featuring extremely high sensitivity, specificity, and reliability (Page 8, lines 15-18). An ordinary practitioner would have been motivated to combine and substitute the chip containing polyamine analogues as therapeutic and diagnostic agents of Vermeulin et al. in the herbal chip of Mao et al., in order to achieve the express advantage, as noted by Vermeulin et al, of the assays of the invention, which are useful for high throughput screening of targets in the discovery of drugs that interact with the polyamine system and also in order to achieve the express advantage, as noted by Mao et al, of the diagnosis chip technique which is a molecular diagnosis method combining DNA hybridization technique and fluorescent marking technique, featuring extremely high sensitivity, specificity, and reliability.

Mao et al in view of Vermeulin et al. do not teach polyfunctional epoxide on the chip that can react with hydroxyl, sulfhydryl or amino groups.

Cruickshank teaches polyfunctional epoxide on the chip that can react with hydroxyl, sulfhydryl or amino groups (Column 7, line 58 to column 8, line 21).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the polyfunctional epoxide on the chip that can react with hydroxyl, sulfhydryl or amino groups of Cruickshank in the herbal chip and method of Mao et al in view of Vermeulin et al., since Cruickshank states, "Surfaces can be functionalized with, for example, amino, sulfhydryl, hydroxyl or epoxide reactive groups that subsequently can be used to attach biochemical ligands to the surface (Column 7, lines 63-66)." An ordinary practitioner would have been motivated to combine and substitute the polyfunctional epoxide on the chip that can react with hydroxyl, sulfhydryl or amino groups of Cruickshank in the herbal chip and method of Mao et al in view of Vermeulin et al. in order to achieve the express advantage, as noted by Cruickshank, of the surfaces functionalized with, for example, amino, sulfhydryl, hydroxyl or epoxide reactive groups that subsequently can be used to attach biochemical ligands (obviously present in herbs) to the surface.

Mao et al. in view of Vermeulin et al. further in view of Cruickshank do not teach the polyfunctional epoxide containing a long chain of 6 to 24 carbon atoms. However, it is *prima facie* obvious that selection of a particular length of carbon atoms in an epoxide molecule in a pharmaceutical composition represents routine optimization with regard to the requirement of the biochemical ligands to be attached to the surface of the chip, which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions

> of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of a particular length of carbon atoms in an epoxide molecule in a pharmaceutical composition was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

4. Claims 3-4 are rejected under 35 U.S.C. 103(a) over Mao et al. (Chinese Patent CN 1314493) (March 20, 2000) in view of Vermeulin et al. (U.S. Patent 6,172,261 B1) (January 9, 2001) further in view of Cruickshank (U.S. Patent 6,194,563 B1) (February 27, 2001) further in view of Chang et al. (U.S. Patent 5,753,692) (May 19, 1998).

Mao et al. in view of Vermeulin et al. further in view of Cruickshank teach the herbal chip and method of claims 1, 2, 5-9, 14-19, and 21-24 as described above.

Mao et al. in view of Vermeulin et al. further in view of Cruickshank do not teach homogeneous fractions or components obtained from herbs by fractionating an extract of the herb by applying HPLC.

Chang et al teach homogeneous fractions or components obtained from herbs by fractionating an extract of the herb by applying HPLC (Column 3, lines 46-60).

Mao et al. in view of Vermeulin et al. further in view of Cruickshank do not teach fractions or components obtained from herbs contain secondary metabolites of a herb.

Chang et al teach fractions or components obtained from herbs contain secondary metabolites of a herb (Column 1, line 48 to Column 2, line 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the fractions or components obtained from herbs contain secondary metabolites of a herb by fractionating an extract of the herb by applying HPLC of Chang et al in the method of Mao et al. in view of Vermeulin et al. since Chang et al. state, "The highly purified thiopenes of the present invention which are found to be particularly useful are bithienyl or terthienyl derivatives and intermediates. A preferred method of isolation or purification is carried out by separation via column chromatography and preferably HPLC. HPLC includes polar solvents such as ethyl acetate and the like. Surprisingly, the extract and the eluate each display significant pharmaceutical activity. For example, particularly the extract from the herb, *Echinops grijisii*, and the column chromatographic eluate by polar solvent, for example, ethyl acetate and ethanol showed significant activities in antiedema and interferon-inducing tests. Highly purified thiopenes are greater than about 90% pure. Pharmaceutical compositions within the scope of the present invention comprise these highly purified compounds in amounts effective to produce anti-inflammatory (e.g., anti-edema), anti-cancer, anti-tumor, anti-viral, anti-bacterial or stimulation of immuno-regulatory activity (Column 3, lines 47-65)." An ordinary practitioner would have been motivated to combine and substitute the fractions or components obtained from

herbs contain secondary metabolites of a herb by fractionating an extract of the herb by applying HPLC of Chang et al in the method of Mao et al. in view of Vermeulin et al.., in order to achieve the express advantage, as noted by Chang et al, of an invention, which provides pharmaceutical compositions comprising highly purified herbal compounds in amounts effective to produce anti-inflammatory (e.g., anti-edema), anti-cancer, anti-tumor, anti-viral, anti-bacterial or stimulation of immuno-regulatory activity.

5. Claims 10 and 20 are rejected under 35 U.S.C. 103(a) over Mao et al. (Chinese Patent CN 1314493) (March 20, 2000) in view of Vermeulin et al. (U.S. Patent 6,172,261 B1) (January 9, 2001) further in view of Cruickshank (U.S. Patent 6,194,563 B1) (February 27, 2001) further in view of Gerster (U.S. Patent 5,714,608) (February 3, 1998).

Mao et al. in view of Vermeulin et al. further in view of Cruickshank teach the herbal chip and method of claims 1, 2, 5-9, 14-19, and 21-24 as described above.

Mao et al. in view of Vermeulin et al. further in view of Cruickshank do not teach ammonium hydroxide as NH2 group(s)-providing precursor.

Gerster teach ammonium hydroxide as NH2 group(s)-providing precursor (Column 7, lines 21-34 and Column 8, lines 31-54).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the ammonium hydroxide as NH2 group(s)-providing precursor of Gerster in the herbal chip and method of Chang et al in view of Vermeulin et al. since Gerster states, "Suitable aminating agents include ammonia (e.g., in the form of

ammonium hydroxide) and ammonium salts (e.g., ammonium carbonate, ammonium bicarbonate, and ammonium phosphate). Ammonium hydroxide is preferred (Column 8, lines 43-47)." An ordinary practitioner would have been motivated to combine and substitute the ammonium hydroxide as NH2 group(s)-providing precursor of Gerster in the herbal chip and method of Chang et al in view of Vermeulin et al., in order to achieve the express advantage, as noted by Gerster, of the suitable aminating agents including ammonia (e.g., in the form of ammonium hydroxide) and ammonium salts (e.g., ammonium carbonate, ammonium bicarbonate, and ammonium phosphate), wherein ammonium hydroxide is preferred.

Response to Amendment

6. In response to amendment, all previous 103 (a) rejections are withdrawn. However, three new 103(a) rejections have been included.

Response to Arguments

7. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703)

306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1634
January 22, 2003

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